Reply to the Editor:

My colleagues and I appreciate the comments by Lin and colleagues regarding potential issues that may influence outcomes in pexelizumab-treated patients. Their hypothesis that pexelizumab may cause platelet aggregation, however, is not supported by the literature. We note that their reference 3 (Røger and colleagues) actually suggested that inhibiting the terminal complement cascade with a molecule such as pexelizumab might inhibit platelet aggregation. The suggestion of Lin and colleagues that this compound's cardioprotective effect may depend on the presence of adequate antithrombotic therapy is an interesting but unproven hypothesis. Unfortunately, Lin and colleagues' suggestion that large amounts of heparin may achieve longer activated clotting times to suppress thrombin activity is also not supported by the literature.[1] We also disagree that as time passes, heparin-bonded circuits may replace the traditional bypass circuits, because the literature is equivocal that reducing perioperative heparin improves safety in cardiac surgical patients. In fact, there is literature suggesting that providing even more systemic heparin might be important in producing less bleeding in cardiac surgical patients.[2,3]

Lin and colleagues is suggested that we reanalyze the Pexelizumab for Reduction of Infarction and Mortality in Coronary Artery Bypass Graft Surgery data with regard to the use of heparin-bonded perfusion circuits, presumably as a surrogate for total heparin dose, to test their hypothesis. We have reviewed the data from the Pexelizumab for Reduction of Infarction and Mortality in Coronary Artery Bypass Graft Surgery II trial, in which 27% of the patients were operated on with heparin-bonded circuits. The primary end point did not differ between pexelizumab and placebo groups (relative risk, 1.02; $P = .9319$). Heparin dosing was not captured in the case report forms.

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COMMENT ON "EFFECT OF STORAGE TIME OF TRANSFUSED PLASMA ON EARLY AND LATE MORTALITY AFTER CORONARY ARTERY BYPASS GRAFTING"

To the Editor:

Plasma from blood donors is frozen and stored at –30°C for a maximum of 2 years. van Straten and colleagues[1] recently reported a 3 times increased 30-day mortality after coronary artery bypass grafting if patients received fresh-frozen plasma (FFP) that had been stored for more than 323 days (old) compared with FFP that had been stored for a shorter time (young). If longer storage of FFP is truly independently associated with a higher mortality, we would need to consider changing the regulations on storage times of FFP. However, before jumping to this conclusion, one needs to carefully consider alternative explanations for the observed association, such as potential biases and confounding.

The design of the study, a cohort among consecutive patients undergoing coronary artery bypass grafting in a period of 10 years, was well chosen, because the choice to transfuse old or young FFP is random. Patients who have received old FFP and patients who have received young FFP can therefore be compared as if from a randomized trial. Table 1 in the report can be used to check whether the randomization was successful. Unfortunately, there are several remarkable differences between the intervention groups, such as the number of patients who underwent reexploration (young FFP 36% vs old FFP 25%) and platelet transfusion (young FFP 0.29 units vs old FFP 0.42 units). Therefore, we conclude that proper randomization was not achieved.

There are several possible explanations for unequal distribution of prognostic factors across the intervention groups. Changes in techniques to produce and store FFP, such as leucodepletion since 2001 and the male-only plasma measure since 2007, have all affected the storage times of FFP during the 10-year period of the study. Therefore, although the choice to

TABLE 1. Time trends in number of patients receiving only young or old fresh-frozen plasma

Year	Only young FFP*	Mixed FFP	Only old FFP*	Total
2004	2 (2.7%)	1 (1.4%)	71 (96%)	74
2005	0 (0%)	4 (1.1%)	365 (99%)	369
2006	5 (1.2%)	20 (4.8%)	390 (94%)	415
2007	120 (27%)	88 (20%)	243 (54%)	451
2008	283 (57%)	121 (25%)	89 (18%)	493
2009	28 (18%)	25 (16%)	103 (66%)	156

FFP, Fresh-frozen plasma. *Only young and only old defined according to van Straten and colleagues[1] at a cutoff of 323 days. Figures represent number of patients and percentages (in parentheses) of the total number of FFP recipients in that year.